

The opinion in support of the decision being entered today is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte RALPH H. WEICHSELBAUM,
DENNIS E. HALLAHAN,
DONALD W. KUFE, and
VIKAS P. SUKHATME

Appeal No. 2006-0141
Application No. 08/289,290
Technology Center 1600

Decided: September 17, 2007

Before HUBERT C. LORIN, TONI R. SCHEINER, and
ERIC B. GRIMES,¹ *Administrative Patent Judges*.

LORIN, Administrative Patent Judge.

DECISION ON REQUEST FOR REHEARING

¹ Administrative Patent Judge Grimes has replaced Administrative Patent Judge Delmendo on this panel. *See In re Bose Corp.*, 772 F.2d 866, 227 USPQ 1 (Fed. Cir. 1985).

INTRODUCTION

Appellants filed a Request for Rehearing (Apr. 12, 2007) contending that the Board, in the Decision on Appeal (mailed Feb. 12, 2007), “did not address Appellants’ arguments regarding the Examiner’s application of the test for obviousness” (p. 1). The arguments Appellants are referring to were originally raised in the Reply Brief (filed Mar. 10, 2005).

In the Decision on Appeal, the Board affirmed a rejection of claims 29 and 37 under 35 U.S.C. § 103 (a) over Zhang and Walther. Among the findings of fact supporting the decision to affirm the rejection was the finding (Finding of Fact 15, Decision on Appeal, p. 6) that “there is no dispute that (a) Zhang discloses an adenovirus construct which may be used to carry genes for cancer therapy other than p53 and (b) Walther discloses a retroviral construct used to carry a gene expressing TNF- α . The table below summarizes the key differences between the prior art and the claimed invention (i.e., Zhang teaches one and Walther the other component of the claimed composition).”

	Zhang	Walther	Claim 29
Nucleic Acid	encodes p53	encodes TNF- α	encodes TNF- α
Vector Construct	adenovirus	retrovirus	adenovirus

This finding was not and is not challenged. Accordingly, there is no dispute that all the limitations of the claimed composition are disclosed in Zhang and Walther. The claimed composition is a combination of a known adenovirus construct (i.e., Zhang) and a known nucleic acid encoding TNF- α (i.e., Walther).

In the Request for Rehearing, Appellants argue, as they did in the Reply Brief, that there is no “motivation to combine” the disclosures of Zhang and Walther (pp. 2-3) and that there is no “reasonable expectation of success” that one of ordinary skill in the art would arrive at the claimed composition given the Zhang and Walther disclosures (pp. 3-5). The Board did consider the Reply Brief in the Decision on Appeal in affirming the rejection (see footnote 2 of the Decision on Appeal). We found the arguments set forth in the Reply Brief unpersuasive as to error in the rejection and, as we explain in more detail below, we continue to find the arguments unpersuasive as to error in the rejection.

DISCUSSION

Motivation to Combine

Appellants contend that “the Board appears to have misapprehended ‘other related genes’ [as set forth in Zhang] to include TNF- α .” Request for Rehearing, p. 3. Appellants go on to argue that the “Decision does not address Appellants’ argument [in the Reply Brief] that TNF- α is not ‘related’ to p53 and antisense oncogenes, which are ‘growth-related’ agents that act on tumors directly. ... Nothing in the present record, or in the art generally, correlates TNF- α as ‘related’ to p53.” Request for Rehearing, p. 3.

We did state in the Decision on Appeal (p. 10) that “Zhang discloses that the adenovirus construct may be used to carry genes for human cancer therapy. FF 5.^[2] The gene expressing TNF- α is a gene for human cancer therapy. FF 12-13.^[3]” We indicated that the disclosure at col. 3, ll. 46-49 of Zhang (“The invention therefore concerns adenovirus vector constructs that involve using Adenovirus to carry tumor suppressor genes such as p53, anti-sense oncogenes *and other related genes for human cancer therapy.*”) supported this statement.

² 5. The examiner (Answer 7) correctly states that “[Zhang] teach[es] an adenovirus construct comprising a nucleic acid that encodes a tumor suppressor gene p53” See Zhang (column 3, lines 46-49), which states:

The invention therefore concerns adenovirus vector constructs that involve using Adenovirus to carry tumor suppressor genes such as p53, anti-sense oncogenes and other related genes for human cancer therapy.

³ 12. The examiner relies on Walther to show that it was well known in the art to form a genetic construct comprising a nucleic acid that encodes TNF- α .

[Walther] ... establish[es] that it is well known in the art [that] a gene therapy vector could be used for encoding and expressing a nucleic acid that encodes TNF- α for the treatment of tumor. [Walther] teach[es] a genetic construct comprising a nucleic acid that encodes TNF- α packaged in a retrovirus particle (paragraph bridging page 1565-66, and 2nd paragraph in left column of 1956).

Answer, p. 8.

13. Walther (p. 1565) discloses that TNF- α is an anti-tumor cytokine that decreases cell proliferation.

In contending that the Board appears to have misapprehended the phrase “other related genes” in Zhang to include TNF- α , Appellants are taking the position that, in disclosing that its invention applies to “related genes for human cancer therapy,” Zhang is referring only to genes that, like p53, act on tumors directly and not to other genes for human cancer therapy, such as TNF- α , which modulate the immune response against tumor cells. However, Appellants have provided no evidence that one of ordinary skill in the art would understand Zhang to be narrowly focused on using an adenovirus with only those genes for human cancer therapy that act on tumors directly. Appellants have provided no evidence that one of ordinary skill would give the term “related” a scope that would confine Zhang’s invention only to those genes having the same *mechanism* to affect human cancer therapy as p53.

Furthermore, the rejection is not over Zhang alone. We clearly stated that “Walther discloses a retroviral vector construct, rather than an adenovirus construct, to carry a gene encoding TNF- α . The gene encoding TNF- α that Walther discloses is useful for human cancer therapy.” Decision on Appeal, p. 10. We went on to explain that “[t]o one of ordinary skill in the art reading Zhang, Walther’s delivery of the gene encoding TNF- α for human cancer therapy would be improved if the retroviral vector that Walther uses in its gene construct was replaced by an adenovirus vector.” Decision on Appeal, p. 10. It was only after establishing that Walther teaches the claimed composition *but for* the use of a retroviral construct that we addressed the added significance of the disclosure in Zhang of “using Adenovirus to carry tumor suppressor

genes such as p53, anti-sense oncogenes *and other related genes for human cancer therapy*.” Appellants do not discuss Zhang and Walther as a whole and therefore have failed to appreciate that the test for obviousness is what the *combined* teachings of the references would suggest to those of ordinary skill in the art. *In re Young*, 927 F.2d 588, 591, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991); *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). Whether or not an individual reference teaches a specific element of the claimed composition is not dispositive of the question of obviousness. Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. *In re Merck*, 800 F.2d 1091, 1097, 231 USPQ 375, 380 (Fed. Cir. 1986); *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981).

Appellants also contend that the “Board did not address Appellants’ argument [in the Reply Brief] that the Zhang reference, at most, suggests that retroviral vectors are problematic for the delivery of p53, or other growth related genes, to cells. ... The Zhang reference does not suggest to one of skill in the art that adenovirus should be used as a substitute for retrovirus for every conceivable therapeutic application of gene therapy using retroviral vectors.” Request for Rehearing, p. 3. We disagree. We clearly observed that Zhang disclosed “major problems [] associated with using retroviral vectors for gene therapy.” Decision on Appeal, p. 10. But, again, in keeping with the rejection over the combination of Walther and Zhang, and not Zhang alone, we found that “[t]o one of ordinary skill in the

art reading Zhang, Walther's delivery of the gene encoding TNF- α for human cancer therapy would be improved if the retroviral vector that Walther uses in its gene construct was replaced by an adenovirus vector." Decision on Appeal, p. 10.

Appellants also attack Walther individually, arguing that "Walther et al., while disclosing delivery of TNF- α to cells via a retroviral vector, make no mention or suggestion that such a retroviral vector would be, or should be, interchangeable with other types of vectors, including adenoviral vectors." Request for Rehearing, p. 3. As the Decision on Appeal makes clear, it is Zhang which suggests using an adenovirus, strengthened by the fact that, as noted above, Zhang further discloses problems with using retroviral vectors.

We would be remiss if we did not also mention the recent development in the law on obviousness as a result of the Supreme Court decision in *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1734, 82 USPQ2d 1385, 1391 (2007). *KSR* issued subsequent to both the mailing of our Decision on Appeal and the filing of Appellants' Request for Rehearing. It clarifies the test for obviousness and has particular relevance to the claims on appeal.

In *KSR*, the Supreme Court emphasized "the need for caution in granting a patent based on the combination of elements found in the prior art," *id.* at 1739, 82 USPQ2d at 1395, and discussed circumstances in which a patent might be determined to be obvious without an explicit application of the teaching, suggestion, motivation test. In particular, the Supreme Court emphasized that "the principles laid down in *Graham* reaffirmed the

‘functional approach’ of *Hotchkiss*, 11 How. 248.” *Id.* (citing *Graham v. John Deere Co.*, 383 U.S. 1, 12, 148 USPQ 459, 464 (1966) (emphasis added)), and reaffirmed principles based on its precedent that “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *Id.* The operative question in this “functional approach” is “whether the improvement is more than the predictable use of prior art elements according to their established functions.” *Id.* at 1740, 82 USPQ2d at 1396.

The question of whether the improvement is more than the predictable use of prior art elements according to their established functions is especially relevant here given the fact that there is no dispute that the adenovirus construct and the nucleic acid encoding TNF- α are known. Appellants have not and could not have argued that these two substances are not disclosed in the prior art. The claims arrange the two substances such that they are combined in a single composition. “When a patent ‘simply arranges old elements with each performing the same function it had been known to perform’ and yields no more than one would expect from such an arrangement, the combination is obvious.” *Id.* at 1739, 82 USPQ2d at 1395 (quoting *Sakraida v. Ag Pro, Inc.*, 425 U.S. 273, 282, 96 S.Ct. 1532 (1976)). In that regard, the record does not include any objective evidence of unexpected results for the claimed combination. No evidence of unexpected results were submitted to rebut the Examiner’s prima facie case of obviousness. Accordingly, a prima facie case of obviousness could have been made on the ground that the claimed composition appeared to be no more than the predictable result of combining Zhang’s adenovirus construct

and Walther's nucleic acid encoding TNF- α according to their established functions.

Accordingly, it was not necessary, as Appellants appear to argue, that the Board show a suggestion to combine the teachings of the references in either Zhang or Walther before coming to the conclusion that the claimed composition would have been obvious to one of ordinary skill in the art. In light of *KSR*, to establish a prima facie case of obviousness under 35 U.S.C. §103(a), it is sufficient to show that the claimed composition is the combination of prior art elements according to known methods to yield predictable results.

That is not to say that all arrangements of prior art elements are necessarily obvious. The Supreme Court made clear that “[f]ollowing these principles may be more difficult in other cases than it is here because the claimed subject matter may involve more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement.” *Id.* The Court explained, “[o]ften, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue.” *Id.* at 1740-41, 82 USPQ2d at 1396. The Court noted that “[t]o facilitate review, this analysis should be made explicit.” *Id.* (citing *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)) (“[R]ejections on obviousness grounds cannot be sustained

by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness”). However, “the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *Id.* at 1741, 82 USPQ2d at 1396. In that regard, we are satisfied that the Decision on Appeal articulated reasoning with sufficient rational underpinning to support the legal conclusion of obviousness.

We have carefully considered the arguments that Appellants have set forth under the topic of a “motivation to combine” (Request for Rehearing, pp. 2-3) but, for the foregoing reasons, do not find them persuasive as to error in the decision to affirm the rejection of the claims under 35 U.S.C. §103(a) over Zhang and Walther.

Reasonable Expectation of Success

Appellants contend that the Board did not address Appellants’ arguments in the Reply Brief wherein Appellants argued that the references do not offer any reasonable expectation of success in making the claimed combination. Appellants concede that the Board considered reasonable expectation of success in reaching the conclusion of obviousness but finds “the Board merely made conclusory statements that one of skill in the art would reasonably expect success.” Request for Rehearing, p. 4.

We disagree that, in the Decision on Appeal, we treated in a conclusory manner the question of whether one of ordinary skill in the art

would have had a reasonable expectation of success in making the claimed combination given the Walther and Zhang disclosures. Appellants list the statements we made on the issue in the Request for Rehearing (p. 4) but neglect to also include the extensive list of facts and analysis that led us to make those statements (Decision on Appeal, pp. 3-13).

Notwithstanding that we clearly addressed the question of a reasonable expectation of success in the Decision on Appeal, it is important to note that, in light of *KSR*, this question is less an issue here where a conclusion of obviousness can be reached using the rationale that the claimed composition is no more than the predictable result of combining Zhang's adenovirus construct and Walther's nucleic acid encoding TNF- α according to their established functions. The question of a reasonable expectation of success plays a greater role in situations where the rationale employs more of an "obvious to try" reasoning – reasoning which we clearly did not rely upon in the Decision on Appeal to affirm the rejection.

Nevertheless, we did explain that "[o]ne of ordinary skill in the art reading Zhang would reasonably expect an adenovirus construct for delivering the gene expressing TNF- α for human cancer therapy to be an improvement over a retroviral vector for doing the same (i.e., Walther)." Decision on Appeal, p. 11.

Appellants challenge our explanation by arguing that we have not provided a legally sufficient basis to support it. Request for Rehearing, p. 4. According to Appellants (repeating what was stated in the Reply Brief), "the choice of viral vector for any particular therapeutic application is dependent on a number of factors that affect the desired outcome" Request for

Rehearing, p. 4. According to Appellants, “one of skill in the art must consider

- whether the polypeptide encoded by the vector construct is likely to interact with viral replication and/or packaging.
- whether viral products may interfere with trafficking or therapeutic function of the polypeptide delivered to the cell.
- whether the host immune response against the viral vector or encoded polypeptide will preclude therapeutic efficacy.”

Request for Rehearing, p. 4. In other words, Appellants are arguing that one of ordinary skill in the art reading Zhang would *not* reasonably expect an adenovirus construct for delivering the gene expressing TNF- α for human cancer therapy to be an improvement over a retroviral vector for doing the same (i.e., Walther) *unless* the variables Appellants have listed above are first considered. We are not persuaded by this argument. We find no evidence supporting Appellants’ contentions elsewhere in the record. *See generally, In re Glass*, 474 F.2d 1015, 1019, 176 USPQ 529, 532 (CCPA 1973); *In re Ludtke*, 441 F.2d 660, 663-64, 169 USPQ 563, 565-67 (CCPA 1971). Appellants’ argument in a brief cannot take the place of evidence. *In re Pearson*, 494 F.2d 1399, 1405, 181 USPQ 641, 646 (CCPA 1974). *See also In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). There is no evidence on record, and Appellants have pointed to none, that show that the level of skill in the art was such that one of ordinary skill in the art would have to have considered all these variables in ascertaining whether to substitute Walther’s retroviral construct for Zhang’s adenovirus for delivering the gene encoding TNF- α . There is no evidence that one of ordinary skill in the art would have needed anything other than the information presented in the references to understand that Zhang’s

adenovirus construct would improve the delivery of Walther's nucleic acid encoding TNF- α , especially given the fact that Zhang discloses the existence of problems associated with the use of retroviral vectors for other genes used in human cancer therapy.

We have carefully considered the arguments that Appellants have set forth under the topic of a "reasonable expectation of success" (Request for Rehearing, pp. 3-5) but, for the foregoing reasons, do not find them persuasive as to error in the decision to affirm the rejection of the claims under 35 U.S.C. §103(a) over Zhang and Walther.

CONCLUSION

Appellants' arguments have been considered but we find them unpersuasive as to error in affirming the rejection of claims 29 and 37 under 35 U.S.C. § 103 (a) over Zhang and Walther.

DENIED

vsh

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